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SCHOOL OF NURSING

Survival and predictors of mortality among children co-infected with Tuberculosis and Human Immunodeficiency Virus at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, 2017. A Retrospective follow-up study

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Lastly, I would like to also thank chronic HIV care clinic staffs of University of Gondar Comprehensive Specialized Hospital.

List of abbreviations

3TC	Lamivudine
ABC	Abacavir
ADIS	Acquired Immunodeficiency Syndrome
AHR	Adjusted Hazard Ratio
AOR	Adjusted Odds Ratio
ART	Antiretroviral Therapy
AZT	Zidovudine
CPT	Cotrimoxazole Preventive Therapy
CY	Child-Year
D4T	Stavudine
EFV	Efaveriniz
Hgb	Hemoglobin
HIV	Human Immune Virus
IPT	Isoniazid Preventive Therapy
IQR	Inter Quartile Range
IRIS	Immune Reconstitution Inflammatory Syndrome
MDR-TB	Multi Drug Resistance Tuberculosis
NNRTIs	Non-Nucleotide Reverse Transcriptase Inhibitors
NRTIs	Nucleotide Reverse Transcriptase Inhibitors
NVP	Nevirapine
OI	Opportunistic Infections
PY	Person-Year
SDG	Sustainable Development Goal
TB	Tuberculosis
TDF	Tenofovir
WHO	World Health Organization

Table of Contents

List of tables

List of figure

List of Annex

Abstract

Introduction: Tuberculosis (TB) and Human immunodeficiency virus (HIV) co-infections are the leading cause of death in children globally, which accounts one-third of death among HIV positive children. However, there are limited studies that assess the survival status and predictors of mortality among TB/HIV co-infected children in Ethiopia.

Objective: This study aimed to determine the survival rate and predictors of mortality among TB/HIV co-infected children enrolled at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia from February 2005 to March 2017.

Methods: A retrospective follow-up study was conducted. Data were extracted from the medical records of the children and entered into EPI-info version 7 then export to STATA version 12 for analysis. Log-rank test was used to compare the survival experience of two or more explanatory variables. A Kaplan–Meier curve was used to estimate the survival time. Bivariabe and multivariable Cox proportional hazards models were fitted to identify the predictors of time to death, with variables having a p-value<0.05 at 95%CI were considered as statistically significant.

Result: Among a total of 271 TB/HIV co-infected children 38(14.02%) children were died during the follow-up period which gives 1167.67 child-years of observations. The overall mortality rate was 3.27(95%CI; 2.3, 4.5) per 100 child-years. The independent predictors of time to death were being age 1-5 years as compared with 1 year(AHR=0.3; 95%CI=0.09-0.98)), being anemic (AHR, 2.6;95%CI,1.24, 5.3), CPT non-users (AHR, 4.1; 95%CI; 1.4, 16.75), IPT non-users (AHR, 2.95; 95%CI; 1.16, 7.5), having EPTB (AHR, 2.43; 95%CI; 1.1, 5.3)) and fair or poor adherence (AHR, 3.5; 95%CI; 1.7, 7.5).

Conclusion: Mortality rate among TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia was high. Age, extra pulmonary tuberculosis, anemia, adherence, CPT and IPT were Independent predictors of mortality. Therefore, those TB/HIV co-infected children, especially those with age less than one year, extra pulmonary TB and anemia should be closely monitored to increase their ART adherence as well as they should be provided with CPT and IPT.

Keywords: TB, HIV, TB/HIV co-infections, survival, mortality, Ethiopia.

1. Introductions

1.1. Statement of the problem

Globally, Tuberculosis (TB) and Human immunodeficiency virus (HIV) co-infections are the first leading cause of death among HIV-infected children (1). Tuberculosis remains a major public health problem especially after the era of HIV (2). It disproportionally affects those peoples living with HIV in low and middle-income countries (2-4). The World Health Organization (WHO) 2016 report estimated that there were 10.4 million new cases of TB globally (equivalent to an incidence rate of 142 cases per 100,000 population) and 1.4 million deaths due to TB in 2015 (5). About 1.2 million cases of those TB cases occurred in HIV-positive peoples and 1.0 million occurred in children. The burden of TB/HIV co-infection is particularly high in developing countries, and approximately 74% of the global TB/HIV co-infection observed in sub-Saharan Africa (6).

Ethiopia is one of the 30 high burden countries and has been classified as having high burdens of TB and TB/HIV co-infection (5, 7) countries. The country is striving to reduce the magnitude of TB and HIV disease in line with the objectives of the sustainable development goal(SDG) (8). However, the problem still remains significant, particularly in children. Several studies had shown that the incidence of TB among HIV-positive children ranges from 1 to 9.9 per 100 PY. TB is also mentioned as one of the top ten causes of death (9) and the most commonly reported opportunistic infection in children with HIV (10-13). In Ethiopia, it is a major cause of hospital admission and death especially in children with HIV (14), accounting for 26% of AIDS-related deaths (15).

TB is a major public health problem in children, the diagnosis of TB in children, particularly in HIV-infected children, is generally challenging (16). Even though, there were advances in the implementation of prevention of mother to child transmission (PMTCT), careful scrutiny for TB exposure at every health care visit, with the provision of isoniazid preventive therapy (IPT) following each documented exposure event in HIV-infected children. In addition, to this, the management of

TB/HIV co-infection in children is very challenging especially in resource-limited counties like Ethiopia as a result of the unavailability of appropriate formulations of drugs, a drug to drug interactions, pill burden, drug side effects and other adherence issues (17).

In 2015, 389,000 people die of globally due to TB/HIV co-infections, of those 295,000 were in Africa. In children, 41,000 children were died due to TB/HIV co-infections. Of them, 34,000 were lived in Africa (5). The mortality rate of TB/HIV co-infection was different in different setting and forms of TB which ranges from 11% to 36.5% (18, 19). The reasons behind the mortality of TB/HIV co-infected children are multi-factorial (20). Which includes diagnosis age, nutritional status, immunity status, and hemoglobin levels at ART initiation (21). The identification of those predictors that determine the mortality rate of TB/HIV co-infected children should allow policy makers and health professionals to implement an integrated program aimed at enhancing the survival of children. This might be particularly important in resource-constrained settings and in high TB/HIV burden countries like Ethiopia to come up with better treatment strategies which will be crucial for TB/HIV co-infections. Hence, the aims of this study were to estimate the survival rate and to identify predictors of mortality among TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia.

1.2. Literature review

1.2.1. Survival of TB/HIV co-infected children

The survival of children co-infected with TB and HIV varies across the globe, as well as within countries, with socio-demographic and a number of other clinical risk factors being strong predictors of mortality (22, 23).

A systematic review and meta-analysis conducted on TB/HIV co-infected children showed that the mortality rate of TB/HIV co-infected children was 11.4% (24). A retrospective cohort study in Thailand showed that the survival rates at 1, 2, and 3 years after TB diagnosis were 96.1%, 94.0%, and 87.7% among on ART user group and 44.4%, 19.2%, and 9.3% among non-ART user group respectively. Among patients on ART user group, the patients who delayed ART initiation ≥6 months after TB diagnosis had a higher mortality rate than those who initiated ART <6 months after TB diagnosis (20). Another cohort study in Thailand also showed that the mortality of incident TB in HIV-infected children was 30% (21).

A cohort study of children in India showed that the mortality rate were 17%, among TB/HIV co-infected children (25). Another similar study conducted in Indian children and adolescent with TB/HIV co-infection who had MDR-TB indicated that 36.5% died of from MDR-TB/HIV co-infections (18).

Similarly, another retrospective cohort study in South Africa showed that the mortality rate was 11% at 18 months after initiation of treatment (19). A similar retrospective cohort study in South African children showed that the overall mortality rate of HIV-infected children with culture-confirmed tuberculosis was 39.1% after completion of TB therapy. From these TB accounts 17.6 % of death (26). Similarly, a retrospective analysis at Durban, South Africa showed that the mortality rate among TB/HIV co-infected children was 17.5%(27).

A retrospective cohort study conducted in Nigerian children showed that the survival rate of children with TB/HIV co-infection was 73.4% (28).

Another retrospective cohort study conducted in Nigeria revealed that a mortality rate of children co-infected TB/HIV was 1.4 per 100 Child-Years (29).

1.2.2. Predictors of mortality in TB-HIV co-infected children

Several predictors have been identified for the mortality of TB/HIV co-infected children in different countries and settings. A retrospective cohort study conducted in the United States of America showed that disseminated and Mengele TB, as well as the absence of TB treatment, were identified as predictors of death among TB/HIV co-infected children (30).

A cohort study conducted in Thailand stated that gastrointestinal TB and multidrug-resistant TB were associated with higher mortality rate. On the other hand, early initiation of ART within six months of TB diagnosis were associated with greater survival (20).

A study in Indian children and adolescent showed that delayed initiation of ART or anti-TB, poor adherence to ART or anti-TB, and defaulted from treatment were the predictors of mortalities among the adolescents (18).

A prospective cohort study conducted among TB/HIV co-infected children in Tanzania identified severe and moderate malnutrition, severe anemia, severe immunosuppression, history of tuberculosis, other opportunistic infections, living in an area with low socio-economic status, and advanced WHO clinical stage was as predictors of mortality in HIV/TB co-infected children (31). A study in Nigerian children showed that children age less 1 year had lower survival rate, with only a survival rate of 29% (28). Another study conducted in Nigeria showed that malnutrition, IPT, delayed ART initiation and age less than 1 year at ART initiation were associated with death among TB/HIV co-infected children (32).

A double-blind randomized control trail at Cape Town, South Africa on the effect of IPT on mortality showed that mortality was lower in the isoniazid group which was 8% than in the placebo group which was 16% (33).

A retrospective cohort study in a regional TB referral hospital KwaZulu-Natal, South Africa, among children reported that mortality of TB/HIV co-infected children was determined by malnutrition, early initiation of TB treatment and severity of tuberculosis (19). A similar study in South Africa showed that early initiation of ART and expanding ART eligibilities were substantially decreased TB-related

mortality in children (34). Another prospective cohort study conducted in South African children showed that Malnutrition and severe radiographic findings were the predictors of death among TB/HIV co-infected children (19). Retrospective cohort study on South African HIV-infected children with culture-confirmed tuberculosis identified that severe malnutrition, age(<1 year), negative tuberculin skin test, HIV disease category and lack of cure at the end of TB therapy were significantly associated with overall mortality (26). A prospective study in South Africa showed that mortality was higher in HIV-1 infected children with tuberculosis than that of HIV-uninfected children and it was associated with late diagnosis and treatment of TB/HIV co-infected children (35).

A prospective cohort study conducted in Malawian children with TB-HIV co-infection stated that severe immunosuppression and WHO Stage IV were significantly associated with mortality. Besides, not initiated on antiretroviral therapy (ART) at any time were 8.8 times more likely to die as compared to those initiated on ART 0-2 months after initiation of anti-tuberculosis treatment (36).

A retrospective cohort study conducted among children diagnosed with TB in Addis Ababa, Ethiopia showed the survival of TB-HIV co-infected children are determined by malnutrition, early diagnosis of TB and adherence with TB treatment (37).

Conceptual framework

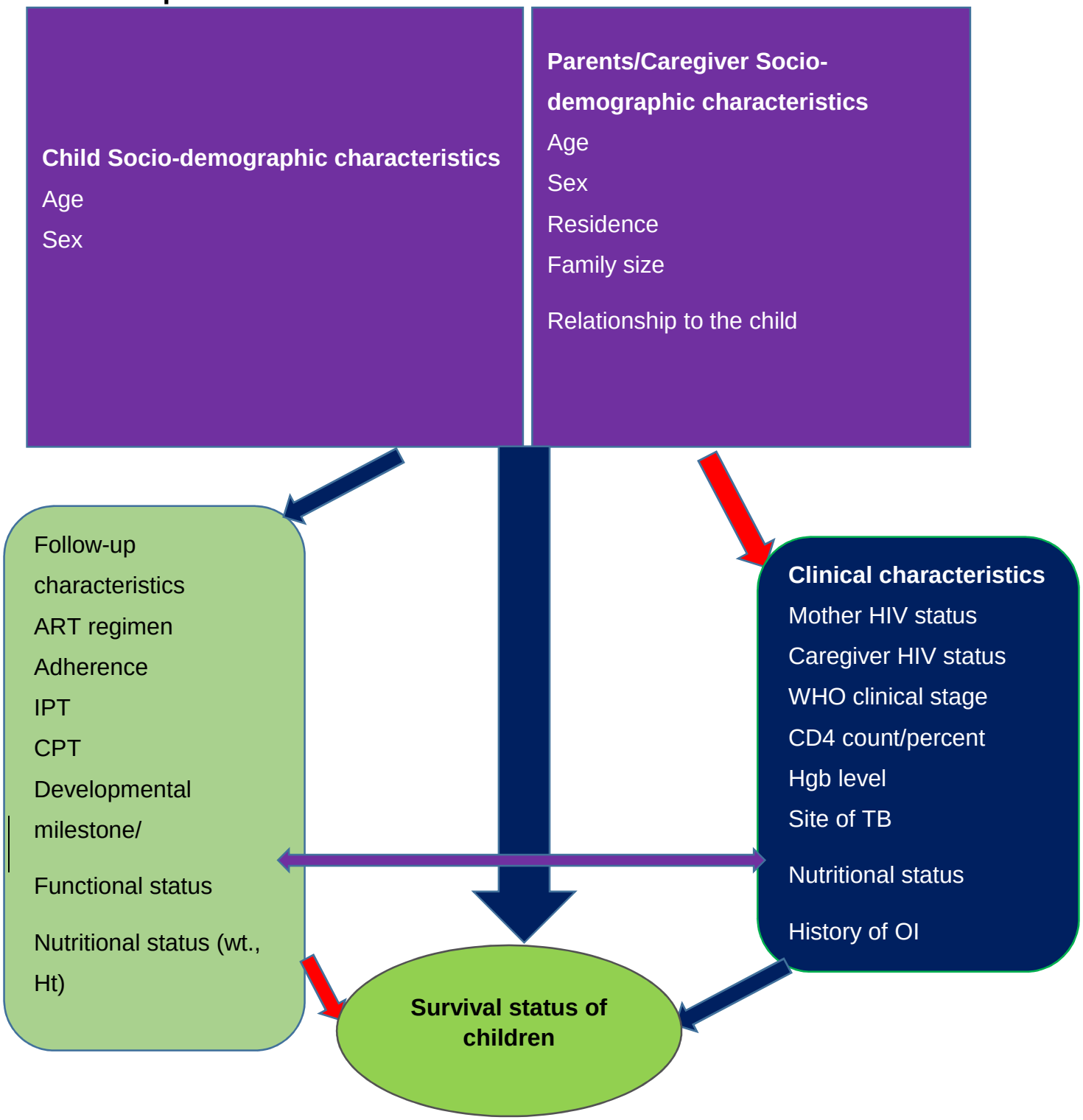


Figure 1 Conceptual framework which shows the survival and predictors of mortality among TB/HIV co-infected children (source; literature review).

1.3. Justification of the study

Tuberculosis and HIV co-infection is the leading cause of death among TB/HIV co-infected individuals may be because of their synergistic effects.

In recent years, great efforts have been made to integrate tuberculosis diagnosis and treatment service into HIV care which is essential to prevent, diagnose and treat TB among people with HIV and HIV among TB patients. However, TB/HIV co-infection remains a major global and national health problem that requires substantial action to achieve the Sustainable Development Goals (SDG) and the END-TB strategies, which targeted to reduce TB death and incidence by 90% and 80% respectively by 2030 compared with 2015. TB/HIV co-infection is especially common in children with age less than 15 years. However, though there are limited studies regarding survival rate of TB/HIV co-infection in adult, data on the survival and predictors of TB/HIV co-infection in children are very limited, particularly in Northwest Ethiopia. Therefore, this study will be important to guide an evidence-based clinical practice, to establish better treatment and preventions strategies in resource-limited settings such as Northwest Ethiopia by assessing the survival of TB/HIV co-infected children and by identifying the predictors of mortality among TB/HIV con-infected children.

2. Objectives

2.1. General objective

- To assess the survival rate and predictors of mortality among TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, from February 2005 to March 2017.

2.2. Specific objectives

- To estimate the survival rate of TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, from February 2005 to March2017.
- To identify predictors of mortality among TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, from February 2005 to March2017.

3. Methods

3.1. Study design and period

An institutional based retrospective follow-up study was conducted at University of Gondar Comprehensive Specialized Hospital pediatric ART clinic from February2005 to March 2017.

3.2. Study area

The study was conducted at University of Gondar Comprehensive Specialized Hospital ART clinic. It is located in North Gondar administrative zone, Amhara National Regional state, Ethiopia which is about 727 km Northwest of Addis Ababa (the capital city of Ethiopia). According to the 2007 population and housing census report, the total population size of Gondar town was estimated to be 206, 987. Currently, Gondar town has one public Comprehensive Specialized Hospital, one private general hospital, five government Health Centers and more than fifty private clinics. University of Gondar Comprehensive Specialized Hospital is a teaching Hospital which serves more than five million people of the North Gondar zone and peoples of the neighboring zones. The HIV care service of the Hospital was initiated in 2005 and has 7 outpatient rooms, one voluntary testing and counseling room, one pharmacy, and one laboratory. In the clinic 2 general practitioners, 2 Health Officer, 8 BSc nurses, 2 masters nurses, 2 masters of infectious disease and HIV medicine, and 20 supportive staff that means case managers and adherence supporters are working there. Adult ART clinic, Pediatric ART clinic, VCT clinic and PMTCT clinic are the specialty clinics in the Hospital. Since 2005 in which the hospital started ART, 8581 adults and 1138 pediatrics patients are enrolled until March 2017.

3.3. Populations

3.3.1. Source populations

The source population was all TB/HIV co-infected children under 15 years age ever enrolled in pediatrics ART clinic at University of Gondar Comprehensive Specialized Hospital.

3.3.2. Study populations

The study population was those under 15 years old children with TB/HIV co-infection who were registered on HIV care and support clinics from February 2005 to March 2017. All TB/HIV co-infected children with age less than 15 years who were enrolled into ART program were followed from February 2005 to March 2017 and followed from date of enrollment to the ART program to the date of the event (i.e. death) or date of the end of data collection (i.e. March 2017).

3.3.3. Inclusion criteria

All TB/HIV co-infected children age less than 15 years who were enrolled in Pediatric ART Clinic at University of Gondar Comprehensive Specialized Hospital from February 2005 to March 2017.

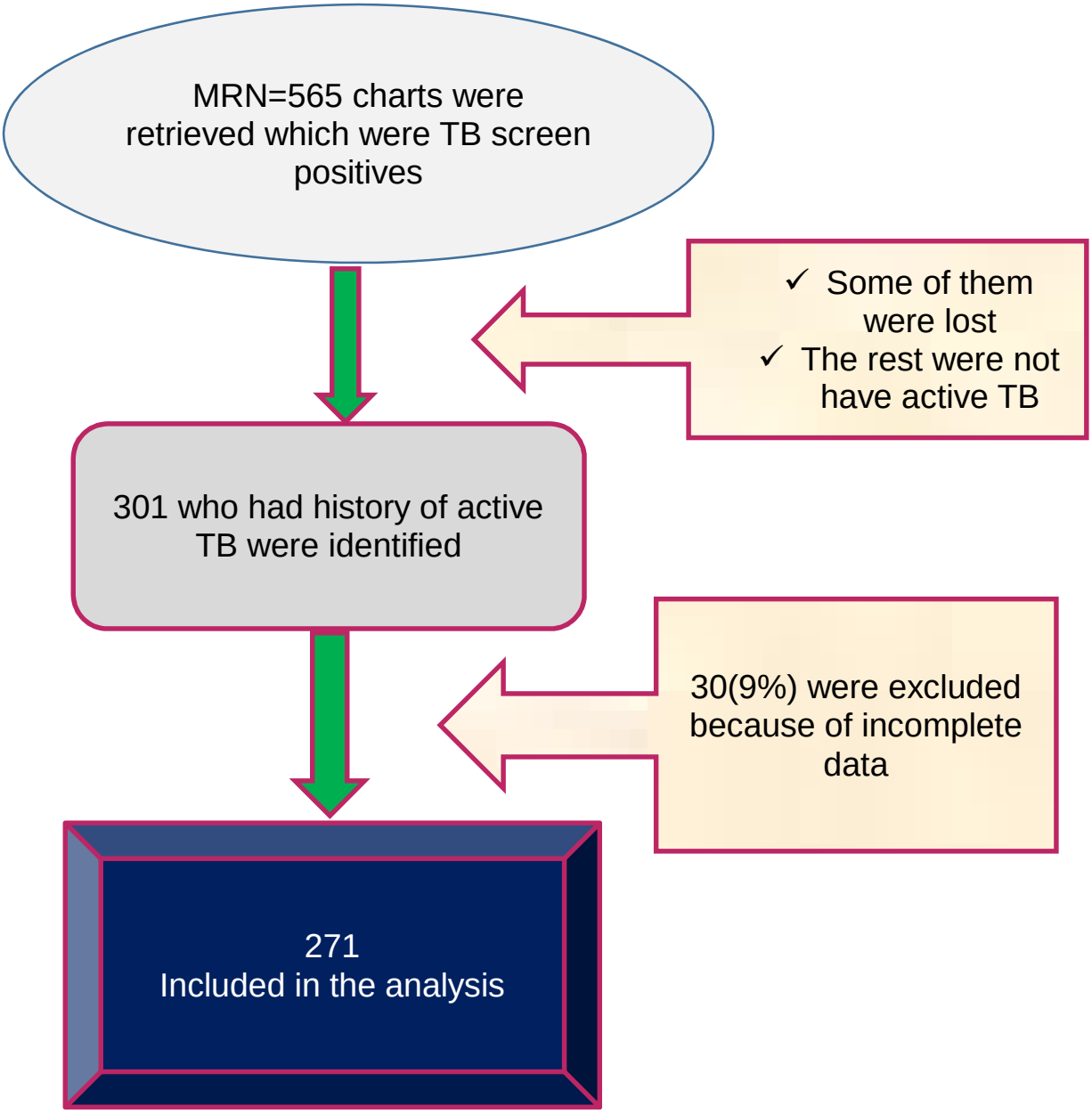
3.3.4. Exclusion criteria

Study participants with incomplete baseline information (i.e. CD4+ cell, WHO stage, Hgb level, Weight, Height, functional status/developmental milestone) were excluded.

3.4. Sample size determination and sampling procedures

The sample size was calculated using Epi info version-7 StatCalc software by assuming 95% CI, a power of 80%, mortality rate 6.2% (29). Using these calculation 244 children were considered. However, since the numbers of TB/HIV co-infected children were small, all children who fulfill the inclusion criteria were included in the study. Medical record numbers of 565 children's charts which had

TB screen positive were identified from the SMART care electronic database of University of Gondar Comprehensive Specialized Hospital ART clinic and retrieved. Finally, after carefully reviewed the chart page by page301 charts with a history of active TB were identified. Of these, 271 fulfill the inclusion criteria and were included in the study.



3.5. Study variables

3.5.1. Dependent variable

Time to death of children with TB/HIV co-infection

3.5.2. Independent variables

Socio-demographic characteristics: -child:-Age and sex.

Care giver: - age, sex, residence, family size, relationship to the child, a child lives with, caregiver HIV status and mother HIV status.

Baseline clinical characteristics: WHO clinical stage, CD4 count/percent, Hgb level, site of TB, Nutritional status and History of OI

The follow-up, clinical and treatment-related characteristics: ART regimen, Adherence, IPT, CPT, Developmental milestone/Functional status, Nutritional status (Weight, Height).

3.6. Operational definition

Time to death: - the time from TB/HIV co-infection to the occurrence of the event (i.e. death) during the follow-up period.

Events – The event of this study was “death” of a child.

Censored – a child was considered as “censored” if the child is lost to follow-up and transfer out to another service before developing the event or if the child alive until the end of the study period that means up to March 2017.

Loss to follow-up- children missing their appointment for follow up or drug pick up for more than three months

Transferred out – those children who were transferred to other health care facilities

Adherence to ART: was classified into good, fair, and poor according to the percentage of drug dosage calculated from the total monthly dose of ART drugs. Which describe as **G**ood (equal to or greater than 95% or ≤ 3 doses missed per

month), **F**air (85- 94% or 4-8 doses missed per month), or **P**oor (less than 85% or ≥ 9 doses missed per month).

Table1: WHO classifications of HIV-associated immunodeficiency in infants and children.

Classification of HIV associated immunodeficiency	Age-related CD4 values			
	<11months	12-35months	36-59months	>=5 years
Non-significant	>35	>30	>25	>500
Mild	30-35	25-30	20-25	350-499
Advanced	25-30	20-25	15-20	200-349
Sever	<25	<20	<15	<200

3.7. Data collection tools and procedures

After carefully observing the available information in the medical records of the children, appropriate data extraction tools were adapted in English from the national HIV intake and follow-up care Form. The data was collected by four nurses working in ART clinic who had ART training, by using the prepared data extraction tools from the children medical records such as pre-ART intake form, ART follow-up form, and laboratory requests etc. Charts were retrieved from the SMART care database which was launched May 2015.

3.8. Data quality control

To maintain the quality of the data, data extraction tool were carefully adapted from the National follow-up care forms and the data was collected by staff nurses who had ART training and working in pediatric ART clinic who are very familiarize with the registration in the medical records of the children. One day training about the objectives, significance, and variables of the research, and how to extract the data by using the data extraction tools was given to four data collectors and two supervisors. The data extraction tool was pretested to check the consistency of the

data extraction tool from the same facilities in about 15 charts. Some charts were checked for completeness before the main data retrieval was started, to modify the data extraction tools based on the available variables. The data collection process was closely monitored by the principal investigator for completeness of the data. Completed questionnaires were checked regularly for completeness to identify the gaps and act immediately.

3.9. Data processing and analysis

After checking the data for completeness and consistency, it was entered into EPI-info version 7 and then exported to STATA version 12 for cleaning, coding and analysis. In the meanwhile WHO Antro-Plus software was also used to classify indices variables or to assess the nutritional status of the child. Descriptive statistics were carried out and summarized using tables, chart and graph. Mortality rate was determined by using Child-Years of follow-up as a denominator for the entire cohort and for groups classified based on socio-demographic and clinical characteristics. Kaplan-Meier curve was used for analysis of probabilities of death. Log-rank test was used to compare survival curves between the different categories of the explanatory variables. A life table was used to estimate the probability of survival at a different time interval in the follow-up time.

Both bivariable and multivariable Cox proportional hazard model were used to identify the predictors of time to death of TB/HIV co-infected children. Variables having p-value less than 0.2 in the bivariable analysis were fitted into the multivariable model. Ninety-five percent confidence interval of hazard ratio were computed and variables having a p-value less than 0.05 in the multivariable Cox proportional hazards model were considered as significantly associated with the dependent variable. The necessary assumption of Cox proportional hazard model was checked by using Schoenfield residuals test.

4. Ethical considerations

Ethical clearance was obtained from the ethical review committee of the school of Nursing, University of Gondar. Permission letter was also obtained from University of Gondar Comprehensive Specialized Hospital's management and HIV care clinics focal person to use the secondary data for the purpose of this study. The name or any other identifying information was not been recorded on the questionnaire and all information is taken from the chart were kept strictly confidential and in a safe place. The questionnaires were kept with locked board and password protected computer was used for the storage to the data. The information retrieved was used for only the study purpose.

5. Results

5.1. Socio-demographic characteristics

A total of 301 TB/HIV co-infected children's charts were reviewed. Of these, 30(9%) were excluded in the analysis due to missing data. Therefore, 271 TB/HIV co-infected children were included in the analysis. The mean age of the study participants was 6.6(±3.5 SD) years. Nearly one-fourth (27.7%) of the children were under 5 years of age and half of them (50.5%) were males. The majorities (80.81%) of the respondent were living in urban and 220 (81.18%) children were lives with their parents. Half (49.82) of children's caregiver were between the age group of (25-34) years with a median age of 30 (IQR (27-38)) years. Approximately, two third (64.94%) of the children's caregivers were HIV positive (Table 2).

Table 2: Socio-demographic characteristics of TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, from February, 2005 to March, 2017. (n=271).

Characteristics		Total N (%) N=271	Death N (%) N=38	Censored N (%) N=233
Age (years)	<1 year	11(4.06)	5(1.85)	6(2.21)
	1-5 year	77(28.41)	8(2.95)	69(25.46)
	6-10 year	125(46.13)	19(7.01)	106(39.11)
	11-14 years	58(21.40)	6(2.210	52(19.19)
Sex	Male	137(50.55)	19(7.01)	118(43.54)
	Female	134(49.45)	19(7.01)	115(42.44)
Age of caregiver	15-24	32(11.81	5(1.85)	27((9.96)
	25-34	135(49.82)	21(7.75)	114(42.07)
	35-44	68(25.09)	7(2.58)	61(22.51)
	>44	36(13.28)	5(1.85)	31(11.44)
Residence	Urban	219(80.81)	28(10.33)	191(70.48)
	Rural	52(19.19)	10(3.69)	42(15.5)
Family size	<=2	44(16.24)	10(3.69)	34(12.55)
	2-4	142(52.40)	18(6.64)	124(45.76)
	>=5	85(31.37)	10(3.69)	75(27.68)
Caregiver of the child	Parents	220(81.18)	31(11.4)	189(69.74)
	Siblings	19(7.01)	1(0.37)	18(6.64)
	Grand-parents	23(8.49)	3(1.11)	20(7.38)
	Others	9(3.32)	3(1.11)	6(2.21)
Child lives with	Parents	247(91.14)	34(12.55)	213(78.60)
	Orphaned	11(4.06)	2(0.74)	9(3.32)
	Others	13(4.80)	2(0.74)	11(4.06)
Mother HIV status	Positive	182(67.16)	22(8.12)	160(59.04)
	Negative	6(2.21)	2(0.74)	4(1.48)
	Unknown	83(30.63)	14(5.17)	69(25.46)
Caregiver HIV status	Positive	176(64.94)	22(8.12)	154(56.83)
	Negative	9(3.32)	3(1.11)	6(2.21)
	Unknown	86(31.73)	13 (4.80)	73(26.94)

5.2. Clinical characteristics

Of the total 271 children, 237(87.46%) of children had advanced baseline WHO stage (3 and 4). The eligibility criteria for initiation of HAART were mainly both CD4+ cell count or percent and WHO clinical stage 125(46%) followed by WHO clinical stage 104(38.38%). Ninety-five (35.06%) of children had experienced initial

regiment change during their follow-up time. Of this, 37(38.95%) were due to D4T phase out followed by Tuberculosis 33(34.74%). Twenty-eight (10.33%) children WHO were on ART had treatment failure. Of them, only 8(28.6%) were on second-line ART.

Forty-eight (17.7%) of the children were anemic at baseline with a median Hgb level 12 (IQR; 10.6–13). Regarding prophylaxis use, 236(87.45%) of the respondents were on co-trimoxazole Preventive Therapy (CPT), whereas, ninety-seven (35.79%) were on isoniazid preventive therapy (IPT). At baseline stunting and underweight were 161(59.41%) and 194(71.59%) respectively (Table 3).

Table3: Clinical characteristics of TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital Northwest Ethiopia, from February 2005 to March 20017. (n=271)

Characteristics		Total N (%) N=271	Death N (%) N=38	Censored N (%) N=233
Baseline WHO stage	I & II	34(12.55)	3(1.11)	31(11.4)
	III & IV	237(87.45)	35(12.9)	202(74.54)
ART Eligibility criteria	CD4+ cell	37(13.65)	4(1.48)	33(12.8)
	WHO stage	104(38.38)	11(4.06)	93(34.32)
	Both	125(46.13)	23(8.49)	102(37.32)
	Not recorded	5(1.85)	0(0)	5(1.850
Initial ART regiment based on NRTIs	ABC-based	10(3.69)	5(1.85)	5(1.85)
	AZT-based	185(68.27)	20(7.38)	165(60.89)
	D4T-based	67(24.72)	12(4.43)	55(20.3)
	TDF-based	9(3.32)	1(0.37)	8(2.95)
Initial ART regiments based on NNRTs	EFV-based	102(37.64)	12(4.43)	90(33.21)
	NVP, PI and other based	169(62.36)	26(9.59)	143(52.77)
Initial regiment change	Yes	95(35.06)	13(4.8)	82(30.26)
	No	176(64.94)	25(9.23)	151(55.72)
Reason for regiment change	Side effect/toxicities	23(24.21)	6(6.32)	17(17.89)
	Treatment failure	2(2.11)	0	2(2.11)
	TB	33(34.74)	5(5.26)	28(29.47)
	Stock out	37(38.95)	2(2.11)	35(36.84)
Treatment failure	Yes	28(10.33)	5(1.85)	23(8.49)
	No	243(89.67)	33(12.18)	210(77.49)

Characteristics		Total N (%)	Death N (%)	Censored N (%)
Immunologic failure	Yes	20(7.38)	4(1.48)	16(5.9)
	No	251(92.62)	34(12.55)	217(80.07)
Virologic failure	Yes	17(6.27)	3(1.11)	14(5.17)
	No	254(93.73)	35(12.92)	219(80.81)
Clinical failure	Yes	5(1.85)	3(1.11)	2(0.74)
	No	266(98.15)	35(12.92)	233(85.24)
Baseline HIV associated Immunosuppression status	Non-significant/Mild	87(32.1)	8(2.95)	79(29.15)
	Advanced	73(26.95)	8(2.95)	65(23.99)
	Sever	111(40.96)	22(8.12)	89(32.84)
Isoniazid	Yes	97(35.79)	6(2.21)	91(33.58)
	No	174(64.21)	32(11.81)	142(52.40)
Hemoglobing/dl	<10	48(17.7)	14(5.17)	34(12.5)
	>=10	223(82.29)	24(8.86)	199(73.43)
Co-trimoxazole preventive therapy	Yes	236(87.08)	28(10.33)	208(76.75)
	No	35(12.92)	10(3.69)	25(9.23)
Weight for age	Normal	77(28.41)	12(4.43)	65(23.99)
	Underweight	194(71.59)	26(9.59)	168(61.99)
Height for age	Normal	110(40.59)	14(5.17)	96(35.42)
	Stunting	161(59.41)	24(8.86)	137(50.55)
Adherence	Good	231(85.24)	23(8.49)	208(76.75)
	Fair	27(9.96)	12(4.43)	15(5.53)
	Poor	13(4.8)	3(1.11)	10(3.69)
Site of TB	PTB	186(68.63)	13(4.80)	173(63.84)
	EPTB	85(31.37)	25(9.23)	60(22.14)
Time at which TB is developed	PRE ART	206(76.01)	25(9.23)	181(66.79)
	ART	65(23.99)	13(4.80)	52(19.19)

Ninety-nine (53.51%), seventy-three (39.46%), and thirteen (7.03%) children greater than 5 years had a functional status of ambulatory, working, and bedridden respectively. Whereas, in children with age less than five years the developmental milestone were 48(54.55%), 37(42.05%) and 3(3.41%) for appropriate, delay and regression respectively.

Among opportunistic infection that occurred at baseline diarrhea 30(22.4%), oral thrush 16(11.9%) and PCP 15(11.2%) contribute nearly half of the opportunistic infections (Figure 2).

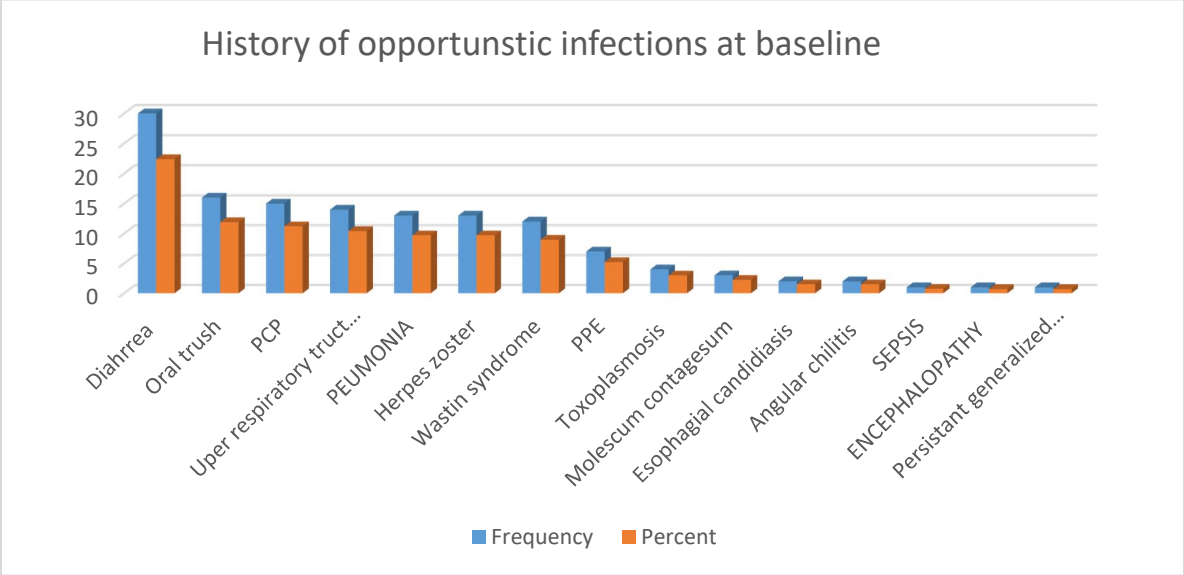


Figure 2: History of opportunistic infections at baseline among TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, from February 2005 to March 2017

5.3. Mortality rate

Two hundred seventy-one TB/HIV co-infected children were followed for different periods which give us 1167.67 Child-Years of observation. Study participants were followed for a minimum of 1 month and a maximum of 12 years, with a median follow-up period of 4(IQR; 1.9-6.5) years. A total of 38(14.02%) new deaths were observed. Hence, the overall mortality rate in this cohort was 3.27 (95%CI; 2.4, 4.5) per 100 Child-Years at 95%CI. Among deaths observed during the follow-up period, exactly 50% were males. Twenty-five of them were extra pulmonary or/and disseminated tuberculosis and HIV co-infected and the rest 13 were pulmonary tuberculosis and HIV co-infected. Twenty-three (60.5%) of deaths occurred within the first year of follow-up.

The cumulative probability of survival at the end of 1 year was 91.2%, at the end of 3 years was 88.6%, at the end of 5 years was 85.8%, and at the end of 12 years was 79.4% respectively. On the other hand, the mortality rate in children less than 1 year was very high (8.92 per 100 Child-Years) as compared with age greater than 1 year (2.99 per 100 Child-Years) (Table 4).

Table 4: Mortality rate stratified by selected socio-demographic and clinical characteristics of TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, from February 2005 to March 2017.

Characteristics		Total N (%)	PY	Death N (%)	IDR
Age (years)	<1	11(4.06)	56.1	5(1.85)	8.92
	>=1	260(95.94)	1105.2	33(12.18)	2.99
Residence	Urban	219(80.81)	1015.25	28(10.33)	2.76
	Rural	52(19.19)	152.4	10(3.69)	6.56
Child lives with	Parents	247(91.14)	1094.58	34(12.55)	3.1
	Orphaned	11(4.06)	36	2(0.74)	5.56
	Others	13(4.80)	37.1	2(0.74)	5.4
Baseline WHO stage	I & II	34(12.55)	114.25	3(1.11)	2.63
	III & IV	237(87.45)	1047	35(12.9)	3.34
Baseline immunity status	Non-significant/Mild	87(32.1)	337.83	8(2.95)	2.37
	Advanced/ severe	184(67.9)	823.42	30(11.07)	3.64
Initial ART regiment based on NRTIs	ABC-based	10(3.69)	20.17	5(1.85)	24.8
	AZT-based	185(68.27)	828.33	20(7.38)	2.4
	D4T-based	67(24.72)	298.17	12(4.43)	4
	TDF-based	9(3.32)	20.99	1(0.37)	4.8
Treatment failure	Yes	28(10.33)	149.58	5(1.85)	3.34
	No	243(89.67)	1018.1	33(12.18)	3.24
Clinical failure	Yes	5(1.85)	12.67	3(1.11)	23.7
	No	266(98.15)	1155	35(12.92)	3
Isoniazid	Yes	97(35.79)	542	6(2.21)	1.1
	No	174(64.21)	625.66	32(11.81)	5.1
Hemoglobin g/dl	<10	48(17.7)	167.58	14(5.17)	8.4
	>=10	223(82.29)	1000.1	24(8.86)	2.4
CPT	Yes	236(87.08)	1079.58	28(10.33)	2.6
	No	35(12.92)	88.1	10(3.69)	11.4
Adherence	Good	231(85.24)	1037.92	23(8.49)	2.22
	Fair/poor	40(14.76)	123.33	15(5.54)	12.2
Site of TB	PTB	186(68.63)	801.67	13(4.80)	1.62
	EPTB	85(31.37)	365.999	25(9.23)	6.83
Follow-up years	<1	44(16.24)	15.33	23(8.49)	150
	1-5	116(42.8)	345.92	9(3.32)	2.6
	>5	111(40.96)	800	6(2.21)	0.75

5.4. Predictors of mortality

Log rank (Mantel-Cox) test of equality of survival for the different categories of explanatory variables were done, and haemoglobin level at TB diagnosis, site of TB infection, CPT use, IPT use and adherence were significantly associated with time to death. The mean survival time of the entire follow-up was 10.2(95%CI; 9.6, 10.7) years among TB/HIV co-infected children.

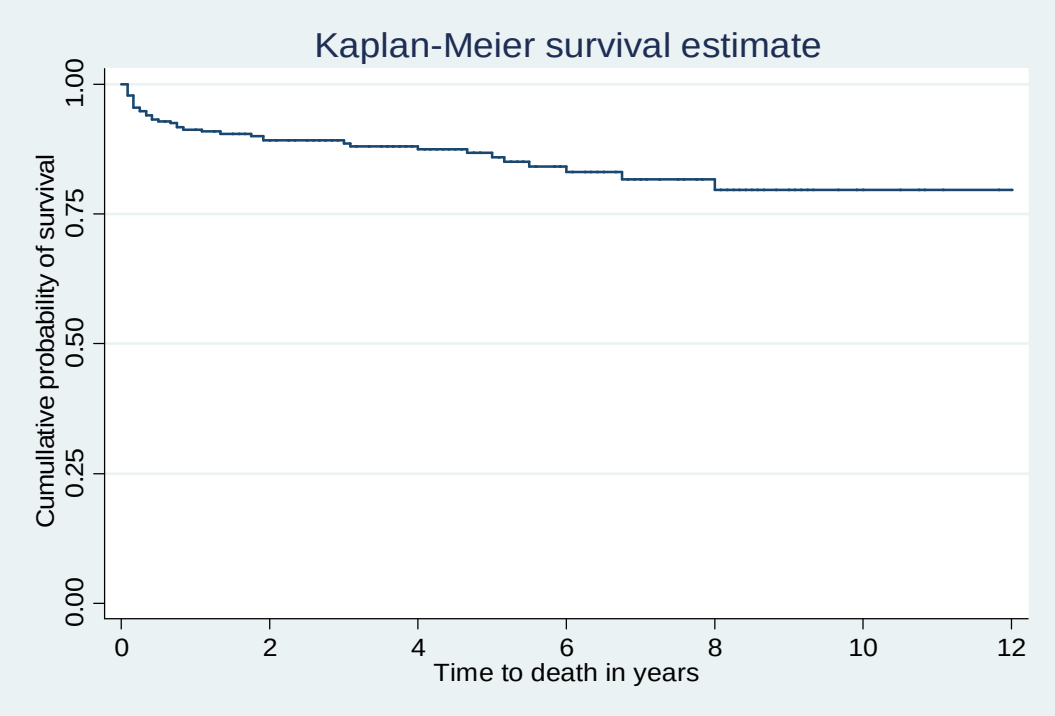


Figure 3: Kaplan-Meier curve of survival proportion for TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, from February 2005 to March 20017.

The mean survival time for those who had hemoglobin level less than 10 g/dl at TB diagnisis was 6(95%CI; 5, 7) years, but for those who had hemoglobin level greater than or equal to 10 g/dl was 10.6(95%CI; 10, 11) years and the difference was significant (p-value=0.0001)

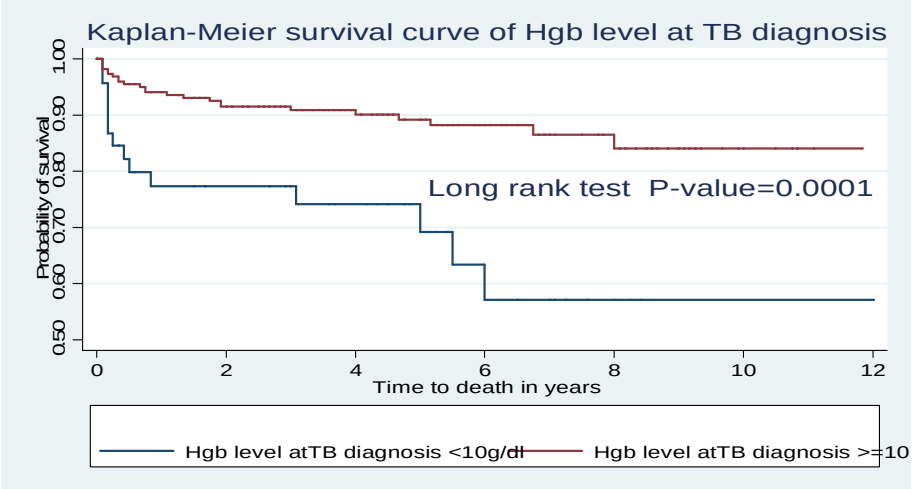


Figure 4: Kaplan-Meier survival estimates of Hemoglobin level at TB diagnosis among TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, from February 2005 to March 2017*.*

The mean survival time of TB/HIV co-infected children for CPT users was high 10.5(95%CI; 9.9, 10.9) years, as compared to non-CPT users 6(95%CI; 4.5, 7.7) years (p-value=0.0004).

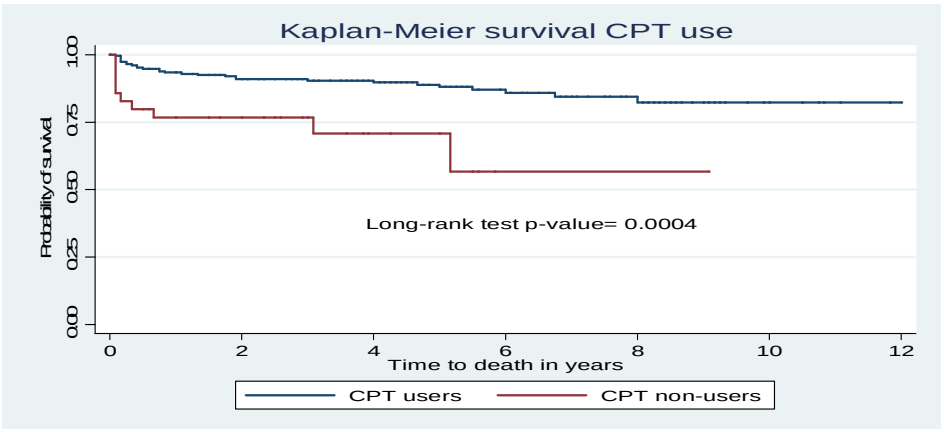
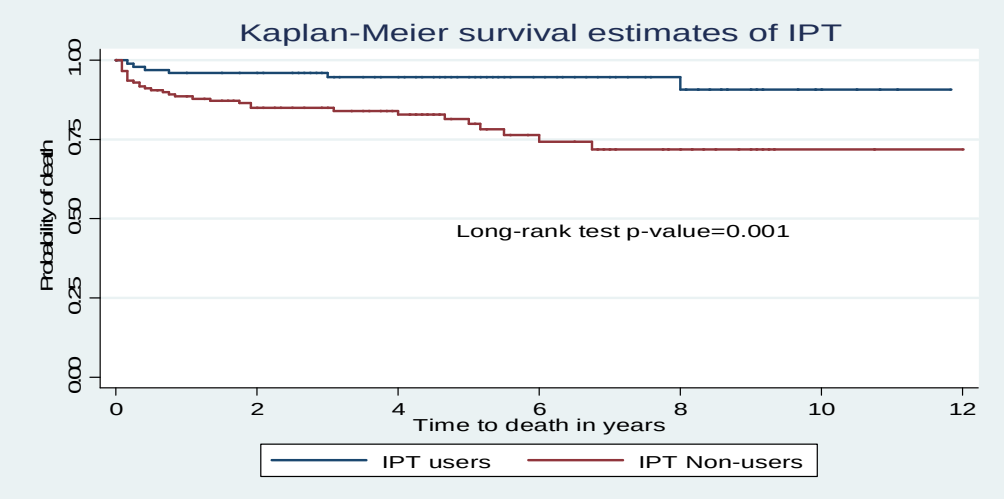


Figure 5: Kaplan-Meier survival curve of CPT use among TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, from February 2005 to March 2017*.*

The mean survival time of IPT users was high 11(95%CI; 10.5, 11.7) years as compared with IPT non-users 9.4(95%CI; 8.6, 10.2) years (p-value=0.001)



Figures 6: Kaplan-Meier survival cure of IPT use among TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, from February 2005 to March 2017.

The mean survival time of children co-infected with TB/HIV who had good adherence to ART drugs was high 10.6(95%CI; 10, 11.2) years as compared to fair or poor adherence 6.9(95%CI; 5, 8.5) years (p-value<0.0001).

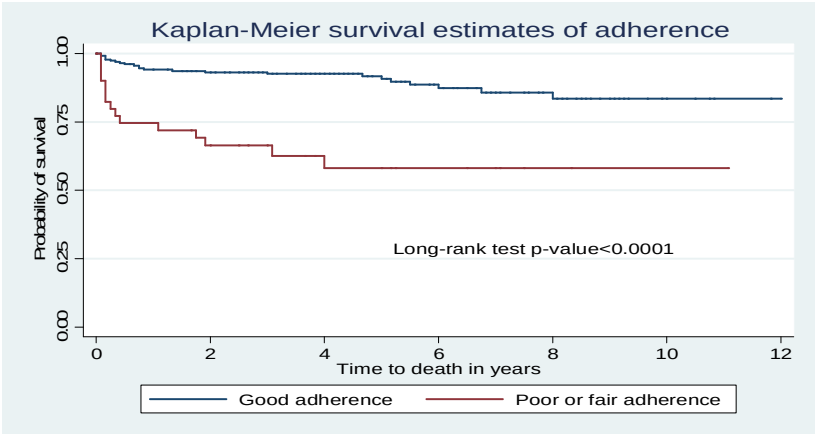


Figure 7: Kaplan-Meier survival curve of ART adherence level among TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, from February 2005 to March 2017.

The mean survival time of children with extra-pulmonary TB was 10(95%CI; 9.5, 10.4) years but it was 8.4(95%CI; 7.2, 9.5) years for those with pulmonary TB and the difference was significant (p-value<0.0001)

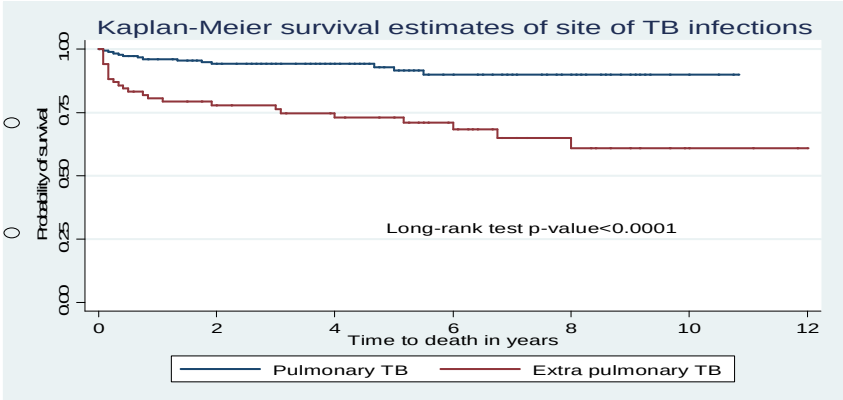


Figure 8: Kaplan-Meier survival cure of site of infection among TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, from February 2005 to March 2017*.*

Cox-regression analysis

The bivariabe Coxregression analysis showed that age, Hemoglobin level, co-trimoxazole preventive therapy (CPT), isoniazid prophylaxis (IPT), site of tuberculosis (TB), severe immunosuppression and adherence to ARV drugs were associated with the occurrence of death among TB/HIV co-infected children. However, in multivariable Cox-regression analysis age, CPT, IPT, site of TB, adherence to ARV drugs and hemoglobin level remained statistically significant predictors of death among TB/HIV co-infected children.

According to our analysis, children whose age group (1-5) years were 70% at lower risk of death as compared with age <1 year (AHR 0.3(95%CI; 0.09-0.98)). Those children whose Hgb level< 10g/dl were 2.6 times at high risk to death as compared to that of Hgb level >=10g/dl (AHR=2.6, 95%CI=1.24-5.3). Similarly, HIV-positive children co-infected with extra-pulmonary or/and disseminated tuberculosis were 2.43 times at high risk of death as compared with HIV-positive children co-infected with pulmonary tuberculosis (AHR=2.43; 95%CI 1.1-5.3). Children who didn't take CPT were 4.1times at high risk to die as compared with CPT users (AHR=4.1; 95%CI=1.76-9.7). Similarly, children who were IPT non-users were 2.95 times at high risk for death as compared with IPT users (AHR=2.95; 95%CI=1.16-7.45).

A child with fair or poor adherence about ART drug was 3.57 times at high risk to death as compared with children who had good adherence to ART drugs.

Table 5: Cox-regression analysis of predictors of time to death of TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia, from February 2005 to March 2017. (n=271).

Characteristics		Death	Censored	CHR(95%CI)	AHR(95%CI)
Age	<1year	5	6	1.00	1.00
	1-5 years	8	69	**0.25 (0.082-0.77)**	**0.3(0.09-0.98)**
	5-10	19	106	0.37(0.14-1.00)	0.7(0.22-2.3)
	10-14	6	52	0.29(0.09-0.96)	0.33(0.084-1.33)
Mother HIV	Positive	22	160	1.00	1.00
status	Negative/Unknown	16	73	1.77(0.93-3.37)	1.14(0.26-5)
Address	Urban	28	191	1.00	1.00
	Rural	10	42	1.99(0.96-4.11)	1.58(0.696-3.6)
HIV status of	Positive	22	154	1.00	1.00
caregiver	Negative /Unknown	16	79	1.57(0.82-2.997)	1.69(0.38-7.5)
Immunity status	N.S & mild	8	86	1.00	1.00
at TB diagnosis	Advanced IS	7	59	1.17(0.42-3.23)	1.3(0.44-3.94)
	Sever IS	23	88	**2.32(1.04-5.199)**	2.45(0.97-6.2)
Hgb level at TB	<10 mg/dl	14	34	**3.1(1.6-6)**	**2.6(1.24-5.3)**
diagnosis	>=10 mg/dl	24	199	1.00	1.00
CPT	Yes	28	208	1.00	1.00
	No	10	25	**3.51(1.68-7.31)**	**4.1(1.76-9.7)**
IPT	Yes	6	91	1.00	1.00
	No	32	142	**3.87(1.6-9.28)**	**2.95(1.16-7.45)**
Site of TB	PTB	13	173		
	EPTB	25	60	**4.43(2.26-8.67)**	**2.43(1.1-5.3)**
Adherence	Good	23	208	1.00	1.00
	Fair/poor	15	25	**4.86(2.5-9.3)**	**3.57(1.7-7.5)**
Time of TB	Pre ART	25	181	1.00	1.00
occurrence	ART	13	52	1.68(0.86-3.29)	1.46(0.68-3.15)

N.S= non-significant, I.S= immunosuppression

6. Discussion

Tuberculosis is the leading cause of death among children co-infected with TB and HIV (15). Hence, this study was aimed at determining the survival rate and predictors of mortality among TB/HIV co-infected children enrolled in pediatric HIV care clinic at University of Gondar Comprehensive Specialized Hospital. The overall mortality rate of TB/HIV co-infected children in this study was 3.27(95%CI;2.4,4.5) per 100Child-Year of follow-up which was slightly higher than a cohort study conducted in Nigeria which was 1.4(95% CI, 0.8,2.3) per 100 Child-Year follow-up) (29).This could be explained by the fact that, unlike this study, the previous one use only children co-infected with pulmonary tuberculosis and HIV. The other reason may be due to the difference in the follow-up period, in Nigeria study it was 5 years follow-up study. Whereas, our study is a 12 years follow-up study. The proportion of death in this study was 14%(95%CI;10,18)which was almost similar to a systematic review and meta-analysis conducted among TB/HIV co-infected children 11.4% (24), a retrospective analysis at Durban, South Africa 17.5% (27), a cohort study conducted in Indian 17% (25), a retrospective cohort study conducted in South African HIV-infected children with culture-confirmed tuberculosis 17.6% (26), and a cohort study conducted in South Africa 11% (19). This fact might be explained by the similarity of TB burden in the general population in those countries, similarity in treatment, care and support strategy. The last but, not the least reason may be all the above-listed countries were high TB and TB/HIV burden countries (5, 7).However, the proportion of death in this study was lower than a cohort study conducted in Thailand incident TB/HIV co-infected children which were 30%(21), and similar study in Indian children and adolescent with TB/HIV co-infection which was 36.5% (18).This might be due to immune reconstitution inflammatory syndrome (IRIS) in Thailand, since most of the death were observed immediately after initiation of ART which increases the prevalence of IRIS(38).The other reason might be the difference in the quality of child care, study period and setting. The high mortality rate observed in Indian might be due

to the severity or category of TB, the study participant were co-infected with MDR-TB and HIV, which might decrease the survival rate and increase the mortality rate.

According to our analysis, the cumulative survival rate in this study was 79.4 %(95%CI; 71%, 85.6%) which is in line with a retrospective cohort study conducted in Nigeria 73% (28). This might be due to similarity in treatment protocol, socio-demographic characteristics, and the similarity in the implementation of TB and HIV treatment, care and support service. The survival rate in our study at 1, 2 and 3 years were 91.2%, 89.1% and 88.6% respectively, which were similar with a cohort study in Thailand 96.1%, 94% and 87.7% at 1, 2 and 3years respectively among ART users, and much higher than 44.4%, 19.2%, and 9.3% among non-ART user group (20). The discrepancy in those of pre-ART may be due to the effect of ART drugs. Anti-retroviral drugs are responsible in viral suppression, which increase the CD4 cell, finally increase the survival of children and decrease risk of death which is supported, by study conducted in Malawi (36).

In this study, highest mortality rate (8.92/100CY) was observed in the first year of follow-up. The pick mortality rate in the first year might be associated with the progression of sub-clinical disease that remains undetected during enrolment and progresses rapidly. Late arrival at health care means late diagnosis one predictor for death among TB/HIV co-infected children supported by study conducted in South Africa (35). The other fact could be Immune reconstitution inflammatory syndrome (IRIS) which is common within 6 months of ART initiation. The result also showed that a high number of children were started ART within the first year of follow-up which increases the probability of IRIS occurrence (38).The other possible reason for increased TB/HIV co-infected children survival with duration of follow-up could be the result of the progressive increase in CD4 cell count which builds the immune system and this may again decrease the viral load across time, finally increase the survival rate.

In multivariable analysis, TB/HIV co-infected children age 1-5 years had 70% lower risk for death as compared with age less than 1 year(AHR 0.3 (95% CI; 0.09-0.98)) which is in agreements with the study conducted in South Africa(26), and Nigeria(

32). The reason could be explained by the fact that, children with age less than one year had immature immune system especially in TB/HIV co-infected children who have the tendency to develop more severe disease. As a result, they become at high risk for death as compared with other age groups.

Anemic children were 2.6 times at higher risk of death than non-anemic children, which were similar to the study conducted in Tanzanian (31), and Malawian (36)TB/HIV co-infected children. This might be due to the effect of anemia on the oxygen intake capacity which had a synergistic effect with tuberculosis and HIV co-infections that increase the prognosis of the disease process which may end-up with death.

In the analysis predictors that were significantly associated with mortality rate were also co-trimoxazole preventive therapy non-users which had 4.1 times at high risk to die as compared with CPT users(AHR=4.1; 95%CI=1.76-9.7).Empirically, this could be due to the fact that the effect of CPT on decreasing most of the opportunistic infections including PCP. Similarly, isoniazid preventive therapy non-users had 2.95 times high risk to death as compared to non-users (AHR=2.95; 95%CI=1.16-7.45), which was in line with a study conducted in Cape Town, South Africa(33) and Nigeria (32). This could be due to the fact that isoniazid preventive therapy greatly reduces the recurrence of TB.

Another important predictor of mortality was extra pulmonary or disseminated TB which had2.43 times at high risk of death than PTB (AHR=2.43; 95%CI=1.1-5.3). The result was similar to a cohort study conducted in United States of America and Thailand (20, 30). It is known that extra-pulmonary TB especially the disseminated one were more severe than pulmonary TB which increase the mortality rate.

Lastly, this analysis indicated that children who had fair or poor adherence to ART drugs had 3.57 times at high risk for death as compared with children who had good adherence (AHR=3.57; 95%CI=1.7-7.5);Similar findings were reported in other studies conducted in Indian(18)and Addis Ababa Ethiopia(37). The reason behind might be when the child takes ART drugs adherently viral replication were

suppressed which result increase in CD4 cells. Finally, increase the survival of children with TB/HIV co-infections. On the other hand, children who were unable to take ART drugs adherently had comeup with many problems such as treatment failure, a resistant strain which resulted in death the final outcome.

7. Limitation and strength of the study

The limitations of this study

Since it was based on secondary data, there were data gaps due to incomplete medical records and poor linkage between ART and TB registers. Those study subjects whose chart was lost were not included in the study which may undermine the result if it is related to death. Due to diagnostic challenges, TB diagnosis was likely underestimated finally it may affect the outcome of the study. Charts were also lost when a patient admitted to the ward. These may also affect the study outcome.

The strength of this study

The study was conducted for a long follow up with a maximum follow-up of 12 years period which enabled us to know the long-term impact of chronic HIV care and highly active antiretroviral therapy on survival of TB/HIV co-infection. The study was conducted during both Pre-ART and ART periods.

8. Conclusion

Mortality rate was high among TB/HIV co-infected children at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. Age, extra-pulmonary tuberculosis, anemia, fair or poor adherence, use of co-trimoxazole preventive therapy, and isoniazid preventive therapy use were statistically significant predictors of mortality among TB/HIV co-infected children.

9. Recommendations

1. **To governmental and nongovernmental organizations;**

- Strengthening, encourage and promote the use of co-trimoxazole preventive therapy, and isoniazid preventive therapy.
- Establish TB/HIV integrated care program at Chronic HIV care clinic to increase the adherences of children to the care.
- Integrated TB/HIV treatment strategies need to be strengthened with early initiation of HAART as recommended in the national guideline.

2. **To Health care providers**

- Close follow-up for children co-infected with tuberculosis and HIV is important especially within the first year of enrollment to the chronic HIV care.
- It would be better to give special attention for children age less than one year, anemia, fair or poor adherence and extra-pulmonary tuberculosis.
- Children have to be screened for extra-pulmonary tuberculosis for early treatments initiation and follow up.
- The adherences of the children should be closely monitored to provide all the necessary counseling about the importance of ART adherence.
- It would be better to provide intensive counseling about ART drug adherence for the caregivers.

3. **For the child/caregivers;**

- Children have to take ART drugs adherently as prescribed by the health care providers.

4. **To Researchers;**

- The impact of late initiation of ART on the survival of TB/HIV co-infected children needed to be studied which was not included in this studies due to the incomplete data file.
- Nationwide multi-center research on survival and predictors of mortality among TB/HIV co-infection children.

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11. Annex

Annex 1: Information sheet

The title of the Research Project: Survival and predictors of mortality among children co-infected with tuberculosis and human Immunodeficiency at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. **A Retrospective cohort study**

Name of Investigator: KendalemAsmare (BSc in Nursing)

Name of the Organization: University of Gondar College of Medicine and Health Sciences, school of Nursing.

Name of the Sponsor: University of Gondar

Introduction: this information sheet is prepared for University of Gondar Comprehensive Specialized Hospital Administration and Hospital HIV care clinic coordinating office. The aim of the form is to make the above-concerned office clear about the purpose of research, data collection procedures and get permission to conduct the research.

The purpose of the Research Project: To assess the survival time and to identify Predictors of mortality among children co-infected TB and HIV in pediatrics HIV care clinic at University of Gondar Comprehensive Specialized Hospital.

Procedure: In order to achieve the above objective, information which is necessary for the study will be taken from HIV care medical record follow-up forms, ART intake forms, and medical history sheet.

Risk and /or Discomfort: Since the study will be conducted by taking appropriate information from medical chart, it will not inflict any harm on the patients. The name or any other identifying information will not be recorded on the questionnaire and all information is taken from the chart will be kept strictly confidential and in a safe place. The information extracted will be kept secured by locked intolocker by key. After the data will be interred into the computer by password. The information retrieved will only be used for the study purpose.

Benefits: the research had no direct benefit for those whose document/ record is included in this research. But the indirect benefit of the research for the participant and other clients in the program is clear. This is because if program planners are preparing predicted plan there is a benefit for clients in the program of getting appropriate care and treatment services for the children with TB/HIV co-infection. Of all, the research work has a paramount direct benefit for health care planners and managers, especially for those on HIV/TB collaborative program planning and management**.**

Confidentiality: to reassure confidentiality the data on the cart will be collected by those individuals who are working on the HIV care clinic in the facility and information will be collected without the name of the clients. The information collected from this research project will be kept confidential and will be stored in a file. In addition, it will not be revealed to anyone except the investigator and it will be kept in key and locked system with computer pass ward.

Person to contact: This research project will be reviewed and approved by the ethical committee of the school of nursing, College of Medicine and Health Science, University of Gondar. If you want to know more information, you can contact the committee through the address below. If you have any question you can contact the Investigator

1. KendalemAsmare, University of Gondar, College of Medicine and Health Science, school of nursing: principal investigator

Cell phone: +251- 09 18519124

E-mail: kedasmar@gmail.com

የመረጃ እና ስምምነት ዉል ቅጽ

የምርምሩ/ጥናቱ ርዕስ ፡

በጎንደር ዩንቨርሲቲ ሪፈራል ሆስፒታል የኤች አይ ቪ ክትትል ባላቸዉ ህጻናት ላይ የሳንባ ነቀርሳ እና ኤች.አይ.ቪ አንድ ላይ ያለባቸዉ ሕጻናት ምን ያክል ይቆያሉ እና ተዛማጅ ምክንያቶችን በተመለከተ

የዋና ተመራማሪ ስም ፡ ክንዳለም አስማረ

የድርጅቱ ስም ፡- በጎንደር ዩኒቨርሲቲ ህክምናና ጤና ሳይንስ ኮሌጅ የነርሲንግ ትምህርት ቤት

ወጭውን የሚሸፍነው አካል፡- ጎንደር ዩኒቨርሲቲ

መግቢያ፡

ይህ የመረጃ እና የስምምነት ዉል ቅጽ የተዘጋጀዉ ለጎንደር ዩንቨርሲቲ ሪፈራል ሆስፒታል አስተዳደር እንዲሁም በሆስፒታሉ ለሚገኘዉ የህጻናት ኤች አይ ቪ ክሊኒክ ክትትል ሀላፊ ነዉ፡፡ ዋና አላማዉም ስለ ምርምሩ ዓላማ ፤ ስለ መረጃ አሰባሰቡ ፤ እንዲሁም ጥናቱን ለማካሄድ ፍቃድ ለማግኘት ከላይ የተጠቀሱት አካላት ግልጽ እንዲሆንላቸዉ ለማድረግ ነዉ፡፡

ጥናቱ የሚካሄድበት ምክንያት፡

የዚህ ጥናት ዋና አላማ በጎንደር ዩንቨርሲቲ ሪፈራል ሆስፒታል የኤች አይ ቪ ክትትል ባላቸዉ ሕጻናት ላይ የሳንባ ነቀርሳ እና ኤች.አይ.ቪ አንድ ላይ ያለባቸዉ ሕጻናት ምን ያክል ይቆያሉ እና ተዛማጅ ምክንያቶችን ለማጥናት ታቅዶ የተዘጋጀ ነዉ ፡፡

አተገባበር

የጥናቱን አላማ ለማሳካት በጎንደር ዩንቨርሲቲ ሪፈራል ሆስፒታል የኤች አይ ቪ ክትትል ባላቸዉ የህጻናት ቻርት ላይ መረጃዉ ይሰመሰባል፡፡

ሊገጥም የሚችል ችግር /አለመመቸት

የተወሰደዉ መረጃ ሙሉ በሙሉ ከቻርት ላይ ብቻ ስለሆነ በበሽተኞች ላይ ምንም አይነት ጉዳት አላመጣም፡፡ የቻርቱ ባለቤት ስምና መለያ ቁጥር ከመጠይቁ ላይ አልተገለጸም፡፡ የተሰበሰበዉ መረጃ በሎከር ተቆልፎ ተቀመጧል ወደ ኮምፒዉተር ከገባ በኋላ ድግሞ በሚስጥር ቁጥር ተቆልፏል፡፡ በተጨማሪም የተሰበሰበዉ መረጃ ለታቀደለት አላማ ብቻ ይዉላል ፡፡

ጥቅሞች

በዚህ ጥናት ተሳታፊ የሚሆኑ ሰዎች በቀጥታ ሊያገኙት የሚችሉት ጥቅም የለም ። ቢሆንም ግን መረጃዉ የኤች አይ ቪ እና ቲቢ ያለባቸዉ ህጻናት ምን ያክል ጊዜ ይቆያሉ እና ተዛማጅ ምክንያቶችን ለማጥናት ይጠቅማል። ከጥናቱ ዉጤት ተነስቶ በሚደረገዉ የፕሮግራም መሻሻል በቀጥታም ባይሆን ተጠቃሚ ይሆናሉ። በቀጥታ ሊጠቅም የሚችለዉ ግን በህጻናት ኤች.አይ.ቪ እና ቲቢ ዙሪያ ለሚሰሩ የጤና ባለሞያዎች እና ፕሮግራም አዉጭዎች ይሆናል።

ሚስጥራዊነት

ለዚህ ጥናት የሚሰበሰበዉን መረጃ ሚስጥር ለመጠበቅ ሲባል መረጃዉ የሚሰበሰበዉ በሆስፒታሉ ዉስጥ በሚገኘዉ የሕጻት ኤች አይ ቪ ክሊኒክ በሚሰሩ ነርሶች ነዉ ። ከዚህ በኋላ የተመረጡት ነርሶች በቻርቱ ላይ የሚገኘዉን መረጃ ይሰበስባሉ ። በሚሰበሰበዉ መረጃ ላይ የታካሚዉ ስም አይተቀስም።የተሰበሰበዉ መረጃም ከጥናቱ ዋና ተመራማሪ እና ረዳቶቹ በስተቀር ለሌላ ለማንኛዉም ሰዉ ግልጽ አይሆንም ። የተገኘዉ መረጃም ለታቀደለት አላማም ብቻ ይዉላል።

ሊያገኙት የሚችሉት ሰዉ

የዚህ ምርምር ፕሮጀክት በጎንደር ዩንቨርሲቲ ህክምናና ጤና ሳይንስ ኮሌጅ የድርጅት ቁጥጥር ኮሚቴ ታይቶ የሚጸድቅ ይሆናል ። የትኛዉንም ዓይነት ጥያቄ መጠየቅ ቢፈልጉ ከዚህ ቀጥሉ የተጠቀሰዉን ግለሰብ ማግኘት እና በማንኛዉም ጊዜ መጠየቅ ይችላሉ ።

1. ክንዳለም አስማረ ፡- ጎንደር ዩንቨርሲቲ ፤ነርሲንግ ትምህርት ቤት፤ዋና ተመራማሪ

የሞባይል ስልክ +251-9 18519124

ኢ-ሜል kedasmar@gmail.com

Annex 2: Data collection tool (questionnaire)

Code No._____

S. N.	Part I: Socio demographic characteristics		Skip to Qn
	Child socio demographic characteristics		
101	Date of enrolment	/ / /DD/MM/YY	
102	Age at enrolment	Months/ year	
103	Sex	1. Male 2. Female	
104	Birth order	_____	
105	Mother HIV status	1. Positive 2, Negative 3. Unknown	
106	Child lives with	1. Parent 2. Guardian 3, Orphan 4. Others	
	Care giver socio demographic characteristics		
107	Age	_____	
108	Sex	1. Male 2. Female	
109	Relationship to the child	1. Mother 2. Father 3. Step parents 4. Sibling 5. Others (specify)_____	
110	Address	1. Urban 2. Rural 3. Not recorded	
111	Family size	_____	
112	HIV status of care giver	1. Positive 2, Negative 3. Unknown	If 2 or 3 skip to 201
113	If positive, is he/she in HIV care?	1. Yes 2. No	
	Part II: base line clinical characteristics		
201	WHO clinical stage	1. I 2. II 3. III 4. IV	
202	CD4+ count/percent	_____(_____%)	
203	Hgb level	_____mg/dl	
205	Weight at base line	(_____)kg	
206	Height/length at baseline	(----------)cm	

207	History of OI	1, No 2, CMV 3, PCP 4,Herpes simplex 5,Kaposi sarcoma 6,Toxoplasmosis 7,Encephalopathy 8,Wasting syndrome 9,Herpes 10,zoster 11,PGL 12, PML 13, EPTB 14 , Candidiasis 15,Diarrhe 16,Pneumonia 17 ,Other specify-------	
	Part III: HIV care/ ART follow up		
301	Date confirmed HIV+	/ / (DD/MM/YY)	
302	ART Eligible date	/ / (DD/MM/YY)	
303	Eligible criteria	1. CD4 cell count 3. Both 2. WHO clinical stage 4. Not recorded	
304	Date ART started	/ / (DD/MM/YY)	
305	Initial Regimen	_____	
306	Was the Regimen changed?	1. Yes 2. No	If 2→ 310
307	When was it changed	/ / (DD/MM/YY) & month -----	
108	New regiment	_____	
309	Reason for regimen change	1. Side effects 2. Treatment failure 3. TB 4. Stock out 5. Others	
310	Did the child had treatment failure	1. Yes 2. No	If 2 skip to 314
311	If yes when?	_____	
312	Type of failure	1. Immunologic 2, virologic 3. clinical	
313	Second line regiment	1. _____	
314	OI prophylaxis	1. Not given 2. Co-trimoxazole 3. INH 4. Fluconazole 5. Others specify----------	
315	Adherence within 3 month of ART initiation	1. Good 2. Fair 3. Poor	
316	Functional status for age greater than 5 years within 3 months	1. Working 2. Ambulatory 3. Bedridden	

317	Developmental milestone for age <5 years within 3 months	1. Appropriate 2. Delayed 3. Regression	
Part IV: Tuberculosis related questions			
401	Time of TB occurrence	1. Pre ART 2. ART	
402	Site of TB infection	1. Pulmonary 2. Extra pulmonary	
403	WHO stage at TB diagnosis	1. III 2. IV	
404	CD4+ cells	_____(_____%)	
405	Hemoglobin at TB diagnosis	_____	

Part IV: Follow up form to be filled

Follow up date	Months on ART	Current status					Weight(kg)	Functional status/developmental milestone (W,A,B)	WHO stage	TB status	INH	OIs	CPT Adh (G,FP)	ART	CD4 count	Hgb (g/dl)
		Alive	Dead	Loss to	Transfer out	Stop								Adh (G,F,P)		

If the patient Dead, drop out, transfer out or stop when was it occurs -------/------/-----DD/MM/YY?

501	Final status	Death 2, Alive 3.Transfer out 4. Loss to follow-up	
502	Final status date from enrolment (in month	_____	
503	Final status date from TB diagnosis (in moths	_____	
504	Periods at which final status occurred	Pre ART 2. ART	

Name of data collector ----------sign ----------date ----------

Name of supervisor _____sign_____date _____

Annex 3: Declaration

I, the undersigned, MSc student declare that this thesis report is my original work in fulfillment of the requirement for the degree of Master of Science in advanced clinical pediatric and child health nursing.

Name: Kendalem Asmare

Signature: _____

Place of submission: School of Nursing, College of Medicine and Health Sciences, University of Gondar.

Date of Submission: _____

This dissertation thesis report has been submitted for examine bored with my/ our approval as university advisor(s).

Advisors

Name	Signature
1. Nigusie Birhan (BSc, MPH)	_____
2. Daniel Tekle (BSc, MSc)	_____